

patients (7%) died: 2 of disease progression and 2 of other causes. Mean and median time-to-progression are 12.1 and 9.8 months respectively (range 2-53).

Conclusion: Re-EBRT using stereotactic approach is a feasible option for local prostate cancer recurrence, achieving tumour control in 45% of the patients and an acceptable progression-free interval. Toxicity of re-EBRT appeared to be very low. Future studies are needed to identify those patients who would benefit the most from this treatment.

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Hypofractionated radiotherapy and androgen deprivation in intermediate risk prostate cancer

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Purpose or Objective: to evaluate the outcomes in intermediate risk prostate cancer treated with hypofractionated radiotherapy (HyRT)

Material and Methods: Between March 2007 and March 2015, 145 patients affected by intermediate risk (T2b-T2c prostate cancer or Gleason Score equal to 7 or pre-treatment PSA value ranging from 10 to 20 ng/mL) prostate cancer were treated with HyRT. The median age at diagnosis was 74 years (range 53-88). A pre-treatment CT scan with 2.5 mm slices was obtained. MRI was used to better delineate the Clinical Target Volume (CTV) when available. The CTV1 included the prostate plus seminal vesicles (SSV) and the CTV2 the prostate alone. Planning Target Volumes (PTV1 and PTV2, respectively) were generated with 8 mm margin in all directions except posteriorly where a 6 mm expansion was adopted in the first 36 patients. A 5 mm expansion in all direction was used in the other patients as daily kv Cone Beam CT was used to verify the patient position because of an implementation of the linear accelerator. A 3D-CRT and a 15 MV photons linear accelerator was used to deliver the treatment. The PTV1 received 43.8 Gy in 12 fractions and the PTV2 received 54.75 Gy in 15 fractions, three times a week in order to avoid an excess of acute toxicity. Neoadjuvant, concomitant and adjuvant ADT was administered for a total of 9 months and was started 3 months before RT.

Results: After a median follow-up of 52.4 months (range 7 to 95 months), 11 patients (7.6%) died, of whom 9 for intercurrent disease and 2 (1.3%) for PCa. The 5-year OS was 90.1% (95%CI 84.2-97.6%) and the 5-year CSS was 98.6% (95%CI 95.4-100%). Fourteen patients (9.7%) developed biochemical recurrence after a median follow up of 30.5 months (95% CI 28.5 to 32.5 months). Of these patients, thirteen (9.0%) had also a clinical detectable disease while the remaining patient presented only biochemical recurrence. The 5y-bRFS was 88.8% (95%CI 82.8-95.4%). Among the 13 patients with clinical recurrence, 7 (53.8%) had local recurrence, 2 (15.4%) developed distant metastases, and 4 (30.8%) had both local recurrence and distant metastases. Acute genito-urinary (GU) toxicity of grade 1 occurred in 74 patients (51.0%), grade 2 in 15 patients (10.3%) and grade 3 in 2 patients (1.3%). Acute gastrointestinal (GI) toxicity of grade 1 were observed in 27 patients (18.6%), grade 2 in 12 patients (8.2%). None developed acute GI toxicity of grade 3 or 4. Late GU toxicity occurred as follows: grade 1 in 51 patients (35.2%), grade 2 in 12 patients (8.2%), grade 3 in 2 patients (1.3%). Late GI toxicity of grade 1 was observed in 18 patients (12.4%), grade 2 in 6 patients (4.1%) and grade 3 in 1 patient (0.7%).

Conclusion: The hypofractionated schedule used is well tolerated with a low rate of acute and late grade gastrointestinal and genitourinary toxicities. Hypofractionation is useful to obtain high rate of tumor control but a longer follow-up is needed for definitive conclusion.

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Contouring guideline optimisation for prostate pts undergoing carbon ions/photons combined treatment

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Purpose or Objective: In the context of the multi-institutional research project "Carbon ions boost followed by pelvic photon intensity modulated radiotherapy for high risk prostate cancer", Contouring Guidelines (CG) for target volumes and Organs At Risk (OARs) were commonly defined based on National/International standards and local experiences. Intra- and inter-institutional variability was evaluated within a contouring dummy-run and a graphical tool was developed to assist the Radiation Oncologists (ROs) in the standardization of the contouring.

Material and Methods: CT and MR images of 5 prostate patients were randomly chosen. Seven ROs belonging to the three Institutes involved in the project were assigned to independently contour targets (prostate (GTV-P), seminal vesicles (CTV-VS) and pelvic lymph nodes (CTV-N) and OARs (rectum (R), bladder (B), femoral heads (FH), small bowel (SB), penile bulb (PB) and anal canal (AC)). The registration between CT and MR images was only used to contour GTV-P and PB. The contours were compared by means of the DICE Index (defined as $2 \cdot (A \cap B) / (A + B)$, where A e B are the volumes in comparison), as provided by the commercial software VODCA (MSS, v.5.4.0). For each structure, the Global DICE Index (GDI) was calculated as the average value for all the ROs and the patients and then compared with the DICE Index of the individual ROs: an individual DICE Index lower than the corresponding GDI (or lower than a threshold value of 0.9 for GDI > 0.9) was recorded as "disagreement" and reported in a graphical tool (Figure 1) that qualitatively shows intra- and inter-institutional variability.

Results: The resulting GDI are reported in Table 1. A visual analysis of the contours on the CT images showed that the poor quality GDI for CTV-VS and AC were due both to a not strict application of the CG by the ROs of the different Institutes and to the small volume of those structures. The other results were instead attributable to random variation in the contouring. The graphical tool clearly showed that inter-institutional variability was predominant compared to intra-institutional variability both for targets and OARs. Nevertheless, some disagreement was found even between ROs of the same Institute.

Table 1 – Mean values and standard deviations of the Global DICE Index for the contoured structures

Structures	Global DICE Index
Prostate	0,87 ± 0,02
Seminal Vesicles	0,49 ± 0,06
Pelvic Lymph Nodes	0,75 ± 0,01
Rectum	0,80 ± 0,02
Bladder	0,959 ± 0,003
Femoral Heads	0,936 ± 0,005
Small Bowel	0,78 ± 0,10
Penil Bulb	0,71 ± 0,02
Anal Canal	0,52 ± 0,06

	A2	A3	B1	B2	C1	C2
A1			GTV-P/CTV-VS	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS
A2			GTV-P/CTV-VS	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS
A3			GTV-P/CTV-VS	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS
(a) Target Volumes			B1	CTV-N	CTV-N	
			B2	GTV-P/CTV-VS/CTV-N	GTV-P/CTV-VS	
				C1	CTV-VS/CTV-N	
	A2	A3	B1	B2	C1	C2
A1			R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC
A2			R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC
A3			R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC	R/SB/PB/AC
(b) OARs			B1	SB/PB	SB/PB	
			B2	R/SB/PB	R/SB/PB	
				C1	SB/PB	

FIGURE 1 – Graphical tool showing the disagreements between ROs belonging to Institute A (A1,A2,A3), B (B1,B2) and C (C1,C2), for target volumes (a) and OARs (b).

Dark grey cells show intra-Institutional variability, whereas the other cells show inter-Institutional variability

Conclusion: The dummy-run showed that the most significant deviations were obtained when ROs did not precisely apply the CG. Such systematic deviations in the contouring could have a dosimetric impact both for target coverage and OAR sparing, especially for particle therapy. The ROs were provided with the developed graphical tool in order to easily identify their deviations and take corrective actions. The graphical tool could also be useful for the optimization of the contouring strategies within individual Institutes. This work was partially funded by Associazione Italiana per la Ricerca sul Cancro AIRC (grant N-14300)

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Adjuvant androgen deprivation therapy and postoperative radiotherapy in prostate cancer: our data

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Purpose or Objective: To evaluate the role of adjuvant androgen deprivation therapy (ADT) in combination with postoperative radiotherapy (PORT) on biochemical-relapse-free-survival (b-NED) and metastatic-progression-free-survival (mts-NED) in high risk prostate cancer patients (pts).

Material and Methods: Between 2004 and 2012 370 high risk prostate cancer pts received PORT : 120 pts had stage pT3a pN0, 150 pts pT3b pN0, 100 pts pT2c/pT3 R1 and post surgical PSA > 0.2 ng/ml detected in 50 pts. Mean age was 72 years (55-78 yrs). PORT on pelvis and surgical bed was delivered in 150 pts while 220 pts were treated on surgical bed. Dose to pelvis was 45-50 Gy, while dose on surgical bed was 66-72 Gy. ADT was administered in 250 pts and consisted of LH-RH analog in monotherapy (70 pts), BAT (60 pts) and bicalutamide 150 mg (120 pts). Timing of ADT ranged six months to 3 years. ADT was administered during and after PORT with a median of 35 months. Kaplan-Mayer b-Ned and mts-Ned survivals, X-square ($p < 0.05$) and paired t-test for univariate and multivariate analyses ($p < 0.001$) were calculated.

Results: Three - hundred were evaluable at 64 months with a median of 5 years. Two groups were identified: ADT (210 pts) and no ADT (90 pts). One-hundred and twenty pts (120) relapsed: 40 pts in the no ADT group (5 with a biochemical relapse and 35 pts with a metastatic relapse) and 70 pts in the ADT group (20 pts with a biochemical relapse and 50 pts with a metastatic). The 5- year biochemical relapse free survival was 80% for ADT group and 78% for no ADT group ($p = 0.34$); the 5-year metastatic progression free survival for ADT group was 82 % vs 65% ($p < 0.05$) for no ADT group. In the

ADT group, radiotherapy dose <70 Gy and PSA >0.2 ng/ml were independent factors related to high risk of biochemical-relapse while metastatic-relapse-free-survival was influenced by primary component 5 of the Gleason Score (GS), no use of LH-RH analog and time of ADT <2aa. In the no ADT group, PSA > 0.2 ng/ml, radiotherapy dose <70 Gy and R1 disease, were factors influencing the biochemical relapse, while metastatic relapse was influenced by a value of 5 in the Gleason Score.

Conclusion: The role of ADT in adjuvant setting prostate cancer is still unclear; our results suggest a benefit of ADT in metastatic-progression-free-survival, especially in case of primary component 5 in the GS, post-operative PSA >0, BAT <2 years.

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Long term patient reported urinary function following external beam radiotherapy for prostate cancer

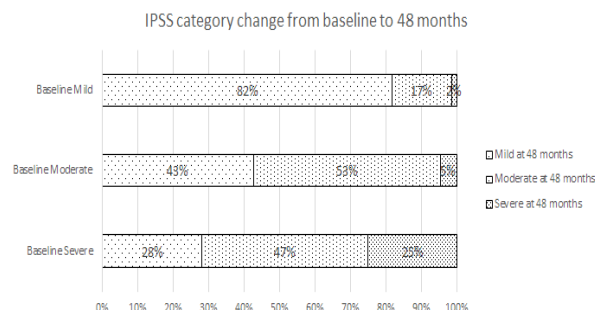
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Purpose or Objective: This study reports long-term patient reported urinary function, toxicity and related quality of life (QoL) after external beam radiotherapy for localized prostate cancer.

Material and Methods: 574 men underwent definitive 3D conformal radiotherapy to 74Gy ± androgen deprivation therapy between 2000 and 2009 with a median follow-up of 42 months. Patients were evaluated at baseline and post treatment using the International Prostate Symptom Score (IPSS) and RTOG CTC.

Results: For patients with mild (48%), moderate (40%) and severe (12%) baseline total IPSS, median IPSS at baseline was 3, 12, and 24. Median IPSS was 4, 9, and 12 at 6 months and 3, 9 and 14 at 48 months respectively. Late grade 2 genitourinary toxicity incidence was 7%, 20% and 33% and late grade 3 genitourinary toxicity was 1%, 2% and 1% respectively. At 48 months, 80%, 49% and 16% of patient with baseline mild, moderate and severe IPSS respectively demonstrated stable IPSS, 5%, 39% and 72% reported improving IPSS ≥5, and 14%, 12% and 6% had a worsening IPSS ≥5. 82% of patients with mild baseline IPSS had mild IPSS scores. 95% of patients with moderate baseline IPSS had mild or moderate IPSS scores, with 43% improving to mild IPSS scores. 75% of patients with severe baseline IPSS scores had improved to mild (28%) or moderate (47%) IPSS scores. 68% of the cohort reported good baseline urinary QoL (score 0-2), with 89% of these patients maintaining good urinary QoL at 48 months. 71% of patients with poor baseline urinary QoL (score 3-6) had improved to good urinary QoL.



Conclusion: The majority of men undergoing definitive radiotherapy for prostate cancer report stable or improving late urinary symptom burden and urinary quality of life, even with severe urinary symptoms or poor urinary quality of life at baseline.